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Original Article

Optical coherence tomography in preoperative workup and visual outcome of pituitary macroadenomas

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ABSTRACT

Background: Pituitary macroadenomas often cause progressive visual loss secondary to chiasmatic or optic nerve compression. At present, there are no precise preoperative evaluation methods capable of predicting postoperative visual outcome. The evaluation of the peripapillary retinal nerve fiber layer (RNFL) and macular thicknesses by optical coherence tomography (OCT) can provide parameters for the severity of optic neuropathy, with possible prognostic value.

Methods: 30 patients were enrolled in this prospective study. Adult patients with sellar preoperative magnetic resonance imaging suggestive of pituitary macroadenomas with suprasellar extensions were included in the study. Patients were evaluated with computerized visual perimetry (VP) and OCT before and after pituitary surgery. Postoperatively, OCTs and VPs were repeated at 30 and 120 days. Surgical procedure consisted of endoscopic endonasal transsphenoidal resection (EETR) of the macroadenoma.

Results: There was a significant improvement in VPs after surgery. Except for two, the thicknesses of the eight sectors of the peripapillary RNFL and the 27 sectors of the three layers of ganglion cell complex of the macula showed no changes postoperatively. All patients with altered preoperative RNFL scans already demonstrated PV abnormalities.

Conclusion: Despite most patients show important perimetric improvements after EETR of pituitary macroadenomas, OCT parameters tend to remain stable, suggesting that postoperative visual recovery is independent of the increase in retinal neuronal layers. Furthermore, OCT is capable of adequately detecting signs of compressive optic neuropathy, but peripapillary RNFL appears to demonstrate no advantage over VP for the early detection of visual compromise in the scenario of pituitary macroadenomas.

Keywords: Endoscopy, Optic coherence tomography, Pituitary neoplasms, Visual fields

INTRODUCTION

Pituitary adenomas, or pituitary neuroendocrine tumors (PitNETs), account for approximately 15% of intracranial tumors,[1] with an estimated prevalence of 96 cases/100,000 individuals.[12] They are classified as micro or macroadenomas, depending on whether smaller or larger than 10 mm in their longest axis. Except for prolactinomas, the treatment of pituitary macroadenomas, when necessary, is preferably surgical. One of the main objectives of the surgical approach is the

decompression of the anterior optic pathways, which provide visual improvement to approximately 70% of the patients postoperatively.[23] It is not clear, however, which patients will show visual improvement after the surgical resection.

Optic coherence tomography (OCT) seems to be a promising resource for measuring the severity of compressive optic neuropathy, with a possible correlation with postoperative visual outcome. This is based on the rationale that true neuronal loss would not allow significant recovery,[19,20] and hence, campimetric or visual acuity (VA) deficits associated with significant retinal neuronal layers thinning on OCT would be poorly recoverable.[11] OCT uses low-coherence tomography, a technique similar to ultrasound – except that it uses light instead of sound, to provide two-dimensional cross-sectional images of structures in the posterior pole of the eye, including the retinal nerve fiber layer (RNFL), the optic papilla and peripapillary region, and the macula.[24] In fact, it was observed that macroadenoma patients with normal RNFL measurements on preoperative OCT had a better visual prognosis, with earlier and more pronounced recovery of acuity and visual fields, while those presenting RNFL thinning preoperatively showed a worse and slower recovery after surgery.[8] Other studies, however, demonstrated some discrepancy between the visual outcome and OCT parameters, with significant visual recovery even in patients who presented preoperative RNFL thinning.[14,26]

Therefore, further studies are needed to better assess the value of OCT in the visual prognosis of patients with pituitary macroadenomas. We believe that the use of specific sectorial peripapillary and macular parameters for patients with compressive optic neuropathy, exclusively secondary to macroadenomas with suprasellar extension and submitted to the same type of surgical treatment, could provide more enlightening data on the importance of OCT in the initial assessment and visual outcome of this specific population.

MATERIALS AND METHODS

This prospective study has been conducted in accordance with the principles set forth in the Helsinki Declaration. It was submitted to the Ethics Committee of the University of Campinas (CEP – UNICAMP) under the number 73271717.3.0000.5404 and was approved on December 18, 2017, according to the Decision 2.443.954, before our research started. All patients included in the study agreed and signed an informed consent after being duly informed about the research procedures and the confidentiality of the collected data.

The study enrolled consecutively thirty adult patients admitted to the Hospital de Clinicas of the University of Campinas (HC-UNICAMP) with pituitary macroadenomas with suprasellar extension who were eligible for endoscopic endonasal resection. The target number of participants was based primarily on the volume of pituitary adenoma surgeries performed at our hospital, without involving a formal sample size calculation. Functioning and nonfunctioning pituitary macroadenomas were admitted. Initially, only one eye from each of the 30 patients was considered. The reason for this initial choice was to avoid bias in the statistical analysis, as some patients could only have one eye included in the study, due to the impossibility of performing OCT with reliable quality on an eye with low VA. When both eyes of the same patient met all the inclusion and exclusion criteria, the eye with the best preoperative VA was selected, since this characteristic should positively influence the quality of the visual perimetry (VP) and OCT examinations, producing more reliable results. In addition, selecting the best eye better serves the principle of standardizing the sample, since for patients with only one eye included in the study due to inclusion and exclusion criteria restrictions, it was always the poorer eye that was excluded. If the VA of both eyes was equal, the eye with the best mean deviation (MD) value according to the total deviation graph of the VP was selected.

In a secondary analysis, we aimed to assess the value of OCT in the early diagnosis of compressive optic neuropathy. For this analysis, we selected both eyes from seven of the 30 patients, all of whom had normal preoperative VP (MD ≥ −2).

Inclusion criteria

- Adult patients (15–80 years old)
- Brain/sellar region magnetic resonance imaging (MRI) compatible with pituitary macroadenoma with suprasellar extension.

Exclusion criteria

- MRI showing no contact of the pituitary lesion with the optic chiasm or optic nerves.
- Results of the anatomopathological examination other than pituitary adenoma/PitNET
- History of previous cranial radiotherapy
- Unreliable computerized VP (false positives, false negatives, or fixation losses >30%)
- Unreliable OCT – image quality index Q (Q score) <20
- Personal history of glaucoma
- Ocular pressure >21 mmHg
- History or fundoscopic finding compatible with diabetic retinopathy or maculopathies
- Presence of papilledema on fundoscopy
- Corrected VA of the assessed eye worse than 0.6.

Ophthalmic evaluation

Patients underwent a full ophthalmological evaluation including VA, slit lamp assessment, ocular pressure

measurement, and fundoscopy between 0 and 90 days before the surgical procedure.

Computerized VP

Between 0 and 90 days before the surgical procedure, all patients underwent VP with the Humphrey Perimeter Commercial Model 750 (Carl Zeiss Inc., Dublin, California – USA), using the Swedish interactive threshold algorithm (SITA) Fast strategy with the Central 30-2 program. Three average values were used to quantify the severity of campimetric involvement, obtained from the *Total Deviation* graph, all expressed in decibels: (1) MD, which is the average of the 74 points of the entire visual field (excluding 2 points of the blind spot); (2) central mean defect (CMD), which is the average of the 16 central points of the visual field, most representative of macular vision;[20] (3) temporal mean defect (MTD), which values the preferential involvement of the temporal fields that are typically observed in chiasmal compressions and is expressed by the average of the 34 points of the temporal hemifield, excluding the two points immediately above and below the blind spot.[21] Figure 1 illustrates the areas of the total deviation graph used to calculate each of the three VP average values employed. After surgery, the test was repeated on two occasions, 30 days and 120 days after surgery.

Neuroimaging

Brain MRI with an emphasis on the sellar/suprasellar region was carried out within 3 months before the surgical procedure for each patient. The scans were interpreted by neuroradiologists and discussed at the ordinary multidisciplinary meeting to determine the therapeutic approach and schedule. The approximate volume of the pituitary tumors was estimated based on Cavalieri's principle[27] and calculated using the formula ¾ π (a/2 × b/2 × c/2), where a, b, and c corresponded to the largest orthogonal measurements of the tumors in the three axes, craniocaudal, anteroposterior, and laterolateral.[16] A CT scan was performed on postoperative day 1 (POD1) (within 24 h), to assess the surgical bed and look for possible postoperative complications. MRI of the sella turcica was performed up to 120 days after surgery to evaluate the extent of the surgical resection and decompression of the optic apparatus.

OCT

All patients underwent spectral-domain OCT (SD-OCT) to study the macular region and the peripapillary RNFL thicknesses between 0 and 90 days before the surgical procedure. After surgery, the examination was repeated 30 and 120 days postoperatively. The OCT scans were carried out by the same neuro-ophthalmologist with experience in this type of procedure, using the Spectralis commercial model (Heidelberg Engineering, Vista, California - USA).

Macular analysis, with a radial scan centered on the fovea, provided thickness measurements of nine sectors for each of the three retinal layers that comprise the ganglion cell complex (GCC): the inner plexiform layer (IPL), ganglion cell layer (GCL), and nerve fiber layer (NFL). The 9 sectors evaluated for each layer were central (C), inner superior (SI), outer superior (SO), inner nasal (NI), outer nasal (NO), inner inferior (II), outer inferior (IO), inner temporal (TI), and outer temporal (TO), as demonstrated in Figure 2.

For the analysis of the peripapillary RNFL, with a circular scan centered on the optic disc, the global average thickness of the peripapillary region (G) and six individual sectors were obtained nasal (N), inferior nasal (Ni), superior nasal (NS), temporal (T), inferior temporal (Ti), and superior temporal (TS). In addition, the peripapillary scan provided the individual thickness of the papillomacular bundle (PMB), located at the edge of the temporal sector, and of particular importance because it contains axons coming from the foveal region and the macular areas located between the fovea and the optic nerve head (30). Figure 3 shows an example of the images and graphs obtained for the peripapillary OCT of each patient.

Endoscopic endonasal transsphenoidal resection (EETR)

Patients underwent EETR of the sellar/suprasellar tumor, using anesthetic and microsurgical techniques that are already well established in the literature[1,4,5] and standardized in our hospital. The surgical procedures were carried out by a multidisciplinary team involving otorhinolaryngologists and neurosurgeons, coordinated by the same surgeons, one an otorhinolaryngologist and the other a neurosurgeon, both with 15 years of experience in this type of procedure. Tumor samples were sent for anatomopathological examination and immunohistochemical analysis. Postoperative care followed the standard protocol for transsphenoidal neurosurgical procedures, involving an initial intensive care unit stay for a minimum of 24 h, followed by a transition to the ward for ongoing care until hospital discharge.

Statistical analysis

The data from the study of computerized VP and OCT parameters had a numerical distribution and were therefore presented by mean (95% confidence interval for the mean) and/or median (95% confidence interval for the median), depending on the normality assigned to the data profile collected. Three periods were evaluated for VP and OCT in relation to the intervention (EETR of the pituitary macroadenoma): (i) preoperative, (ii) 30 days after intervention, and (iii) 120 days after intervention.

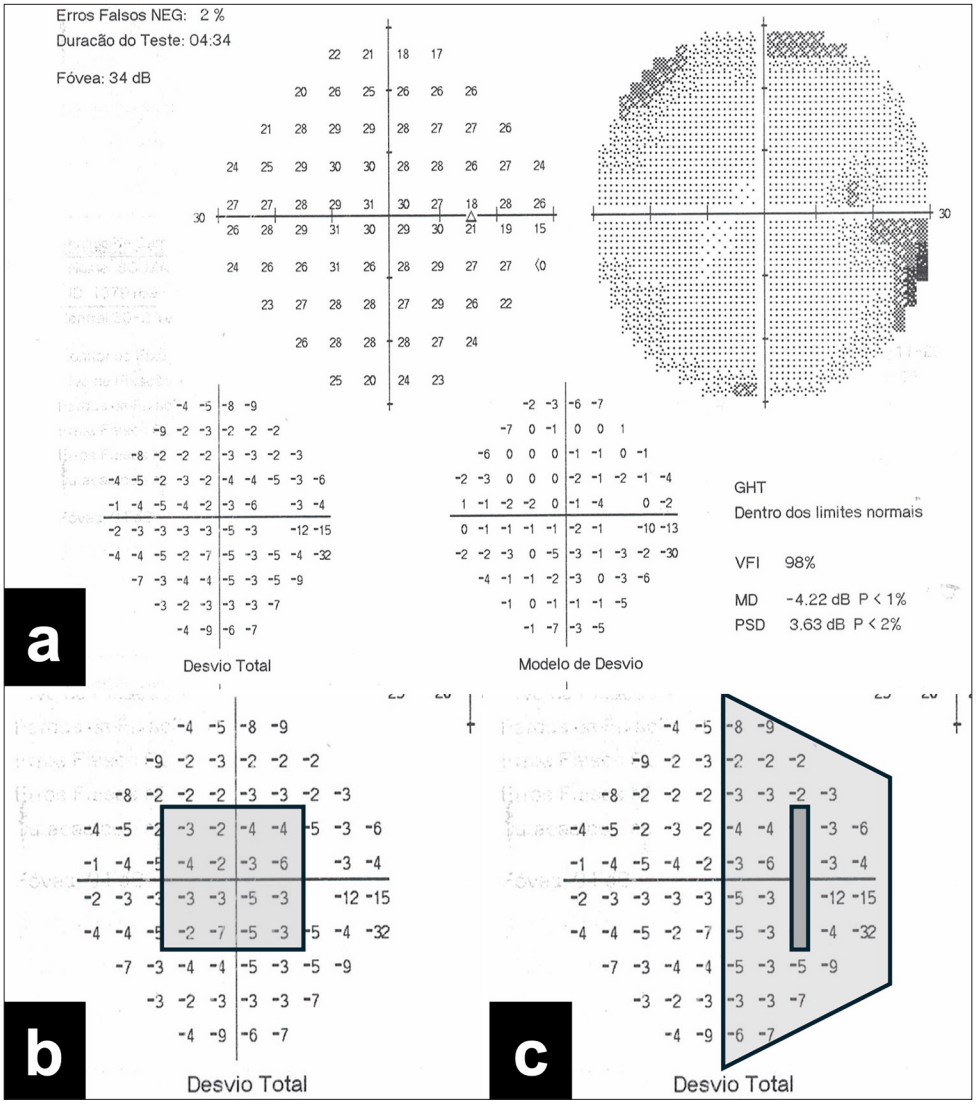


Figure 1: Computerized visual perimetry of the right eye obtained by Humphrey's Perimeter using the SITA-Fast strategy with program 30-2. (a) Mean deviation parameter, expressed on the right, which corresponds to the average of all the values in the Total Deviation graph, expressed in decibels. (b) Demarcated area of the 16 central points used to calculate the average corresponding to the central mean defect. (c) Demarcated area of all the points in the temporal field, excluding the points immediately above and below the blind spot, used to calculate the average corresponding to the temporal mean defect.

Two statistical tests were used to assess the association between the VP and OCT parameter values in relation to the data collection periods - paired analysis: (i) analysis of variance (ANOVA) test for repeated measures (used in the presence of normality in data distribution) and (ii) Friedman's rank analysis of variance test for samples with repeated measures (used in the absence of normality in data distribution). For the ANOVA test, the *P*-value obtained was corrected by a conservative measurement using the Greenhouse–Geisser test in the absence of data sphericity assessed by the Mauchly test. Finally, in the *pairwise* analysis (analysis of paired data), the Bonferroni correction was used as it is a conservative measure for adjusting multiple statistical associations.

The correlation between the VP and OCT parameters in relation to the data collection periods was carried out using Spearman's correlation test. For the qualitative assessment of the degree of Spearman's correlation between the two variables, the following criteria were adopted according to the correlation coefficient (CC) obtained: null or nonexistent (CC = 0–±0.30); weak (CC = ±0.30–±0.50); moderate (CC = ±0.50–±0.70); strong (±0.70–±0.90); and very strong or full/perfect (±0.90–1.00).[22] The respective

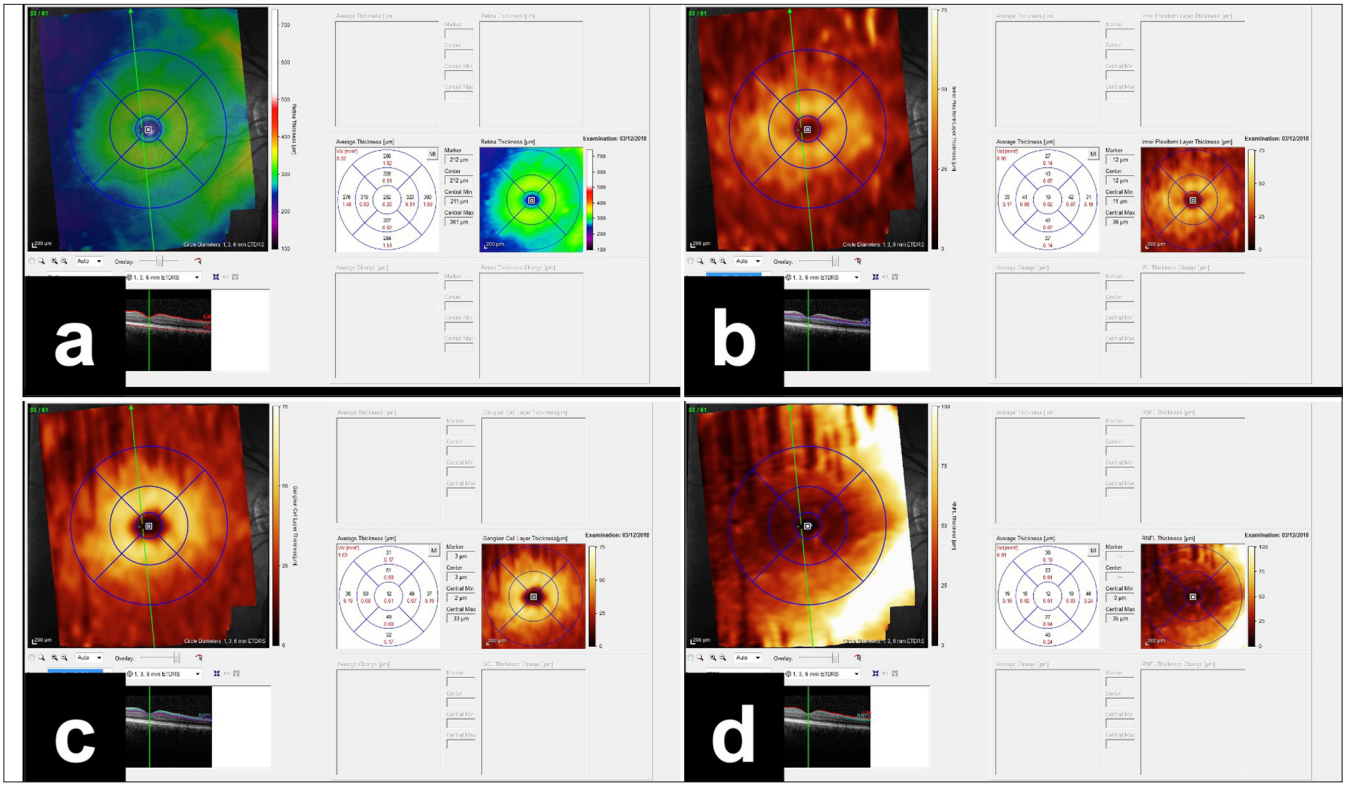


Figure 2: Radial scan of the macula of the right eye, centered on the fovea, obtained by spectral-domain optical coherence tomography. (a) Scan of the entire retinal thickness of the macular region, including cross-sectional image and graph representing 9 macular sectors: Central (C), inner superior (SI) and outer superior (SO); inner nasal (NI) and outer nasal (NO); inner inferior (II) and outer inferior (IO) and inner temporal (TI) and outer temporal (TO). (b-d) Same scan of the macular region now individualizing the thickness of each of the 3 layers of the Ganglion Cell Complex, respectively: Inner plexiform layer, ganglion cell layer, and nerve fiber layer.

95% confidence intervals were presented for the CCs obtained.

Descriptive statistics and inference were analyzed using the Statistical Package for the Social Sciences (SPSS) software (IBM SPSS Statistics for Macintosh, Version 28.0). An alpha error of 0.05 was adopted in all the statistical analyses carried out in this study.

Data availability

The complete data related to this manuscript are not publicly available but can be accessed by contacting the corresponding author.

RESULTS

Forty-two patients were initially included in the study. The first surgical procedure to resect the pituitary tumor in this series took place on September 11, 2018, and the last on September 27, 2022. Of these 42 patients, 12 were excluded for different reasons: three patients did not achieve the minimum preoperative VA in either eye; four patients did not show up for the postoperative ophthalmological examinations; three patients had their preoperative OCT data damaged during the technical maintenance of the device; two patients were excluded due to anatomopathological result other than adenoma/PitNET (first case: metastasis of adenocarcinoma; second case: necrotic tissue without anatomopathological characteristics that could confirm PitNET). Enrolment was completed once 30 patients had been recruited. Nineteen were male and 11 were female. The average age at the time of surgery was 48.2 years, ranging from 16 to 69 years. Table 1 summarizes the main characteristics of the 30 patients, while Figure 4 demonstrated case illustration that illustrates one patient of this series, comparing the main pre and postoperative ophthalmological and neuroimaging results.

Computerized VP

The postoperative evolution of the perimetric values showed a significant improvement in the three average parameters evaluated, both at 30 and 120 days postoperatively, as detailed in Figure 5.

OCT

The analysis of retinal thickness by OCT provided eight parameters of the peripapillary RNFL: one global average value

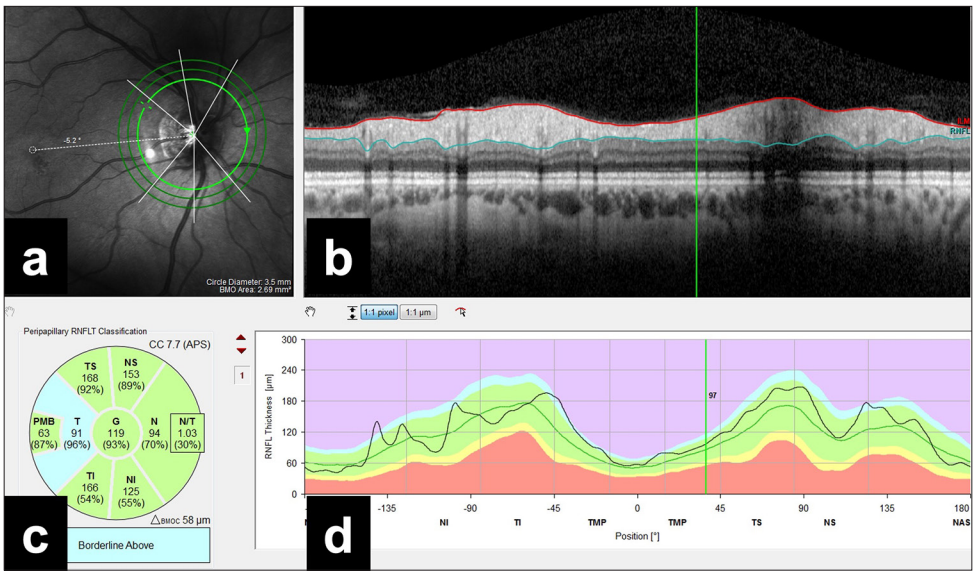


Figure 3: Scan of the nerve fiber layer (RNFL) of the peripapillary retina obtained by spectral-domain optical coherence tomography. (a) Peripapillary scan area centered on the optic nerve head. (b) Cross-sectional image of the peripapillary scan delimiting the RNFL between the green and red lines. (c) Diagram of the thickness compared to normative data, color-coded, of the peripapillary RNFL: Global average value (G), PMB (papillomacular bundle), and the 6 sectors, Superior Nasal (NS), Nasal (N), Inferior Nasal (Ni), Inferior Temporal (Ti), Temporal (T), Superior Temporal (TS). (d) Cross-sectional graphic representation of the thickness of the different sectors of the peripapillary RNFL using the same color code.

(G), six individualized values for each radial sector (NS, TS, Ti, T, Ni, N), and the PMB. The analysis of the retinal thickness of the macular region included one central sector (C) and eight radial sectors (SI, SO, NI, NO, II, IO, TI, TO) for each of the three component layers of the GCC (IPL, GCL, RNFL), totaling 27 macular parameters. There were no significant changes in most of the OCT parameters when comparing the different postoperative times with the preoperative exam, except for the SI and NI sectors of the macular NFL, as shown in Table 2.

Correlation of VP with peripapillary and macular sectors at different times

We tested, at different times (preoperative, PO30, and PO120), the relationship between the thicknesses of all peripapillary RNFL and macular sectors obtained by OCT and the parameters CMD and TMD from VP, which are considered more clinically relevant for chiasmatic compression than MD values. Thickness values of several macular and peripapillary RNFL sectors obtained by OCT demonstrated significant positive correlations with perimetric results at each time point. Peripapillary RNFL-positive correlations were more prominent for the average measure (G), the nasal sectors (N, Ni, and NS), and the PMB. Regarding the macular analysis, the nasal (NI and NO) and inferior (II and IO) sectors of the GCL and IPL exhibited the most significant positive correlations, which were also present, although to a lesser extent, in the NFL. Some other positive correlations were occasionally found in other sectors, such as the temporal (T) and central (C) sectors. A detailed description of all the correlations obtained can be found in the appendix [Supplementary].

In a secondary analysis to investigate whether OCT could detect signs of compressive optic neuropathy before the functional changes detectable in VP, a total of 14 eyes (of seven patients) with a preoperative VP considered normal (MD ≥ -2), were assessed. We analyzed the preoperative peripapillary RNFL based on the color scale provided by the OCT-Spectralis, which compares the values obtained to the device's internal database. Mild alterations were found in 4 eyes, involving sectors G, T, Ti, Ni, and PMB. However, when we reassessed the VP of these eyes, they all showed localized alterations in the gray maps and in the Total Deviation graph, even though the overall MD was within the normal range. This observation indicates that, in such cases, peripapillary RNFL analysis through OCT was unable to detect abnormalities before perimetry. The macular sectors of the OCT could not be incorporated into this analysis as the device does not offer a direct normative reference for these segments.

DISCUSSION

The patients evaluated in this study showed a significant improvement in their perimetric parameters after pituitary

Table 1: Main characteristics of the 30 patients included in the study.

	Name initials	Age	Gender	Endocrine diagnosis	Tumor volume in cm^3	VA RE	VA LE	PitNET AP/IH - description
1	AVS	47	M	Nonfunctioning	24.56	0.9	Amaurosis	Unusual IH combination
2	CEAS	53	M	Nonfunctioning	34.65	1	1	Gonadotropic
3	KNAD	38	F	Nonfunctioning	3.95	1	1	Sparsely Granulated Somatotropic
4	JSF	64	M	Nonfunctioning	17.,26	0.9	0.6	Gonadotropic
5	EPRL	39	F	Nonfunctioning	4.61	0.8	HM	Sparsely Granulated Somatotropic
6	AJPC	69	M	Nonfunctioning	7.89	Amaurosis	0.7	Gonadotropic
7	LM	62	F	Nonfunctioning	8.61	0.2	0.6	Gonadotropic
8	SCM	49	F	Nonfunctioning	11.25	1	1	Gonadotropic
9	MASS	44	F	Cystic Nonfunctioning	2.54	1	1	Gonadotropic
10	MAMH	41	M	Nonfunctioning	20.72	1	0.8	Gonadotropic
11	MDMP	37	F	Prolactinoma+Apoplexy	8.64	HM	0.6	Lactotropic
12	ACS	37	M	Nonfunctioning	24.59	0.9	0.4	Gonadotropic
13	MPSS	43	F	Nonfunctioning	2.15	0.6	0.2	Gonadotropic
14	CE	68	M	Nonfunctioning	7.78	0.6	LP	Gonadotropic
15	ACL	28	M	Nonfunctioning	29.29	1	0.8	Unusual IH combination
16	AAMJ	38	F	Prolactinoma	16.05	0.8	1	Lactotropic
17	JOP	59	M	Nonfunctioning	6.24	0.6	0.7	Gonadotropic
18	PJS	67	M	Nonfunctioning	3.24	0.2	0.8	Gonadotropic
19	GS	45	M	Nonfunctioning	119.17	0.9	0.9	Gonadotropic
20	DN	52	M	Nonfunctioning	3.75	0.8	0.4	Gonadotropic
21	SH	61	M	Nonfunctioning	7.61	0.8	0.2	Gonadotropic
22	JFS	16	F	Cushing	0.57	0.9	0.8	Corticotropic
23	AFSN	61	M	Nonfunctioning	7.21	1	0.6	Gonadotropic
24	TCS	39	F	Cushing	6.51	1	1	Crooke cells Corticotropic
25	PYORP	24	M	Acromegaly	4.59	0.9	1	Densely Granulated Somatotropic
26	CEAP	40	M	Nonfunctioning	7.52	1	1	Apoplexy
27	WAF	44	M	Nonfunctioning	7.68	0.6	HM	Gonadotropic
28	JVL	72	M	Nonfunctioning	10.85	0.8	0.2	Gonadotropic
29	SMRS	44	F	Acromegaly	1.92	1	1	Mammosomatotropic
30	JRO	53	M	TSH-Secreting	25.75	0.7	0.9	Plurihormonal

HM: Hand motion, LE: Left eye, LP: Light perception, NF: Nonfunctioning, PitNET: Neuroendocrine pituitary tumor, RE: Right eye, TSH: TSH-secreting PitNET, VA: Visual acuity

macroadenoma endoscopic endonasal resection. This result corroborates the findings in the literature which point to a significant postoperative visual improvement in the majority of patients with compressive optic neuropathy caused by pituitary macroadenomas or other space-occupying lesions in the sellar region,[10] an improvement that usually occurs mainly in the days to weeks following surgical decompression of the optic apparatus.[11] A recent series of 105 patients who underwent transsphenoidal resection of pituitary macroadenomas over a period of 11 years showed that 92% of patients had improved visual fields in the postoperative period.[28] In terms of surgical technique, endoscopic endonasal transsphenoidal surgery has gained popularity within the neurosurgical community over the past

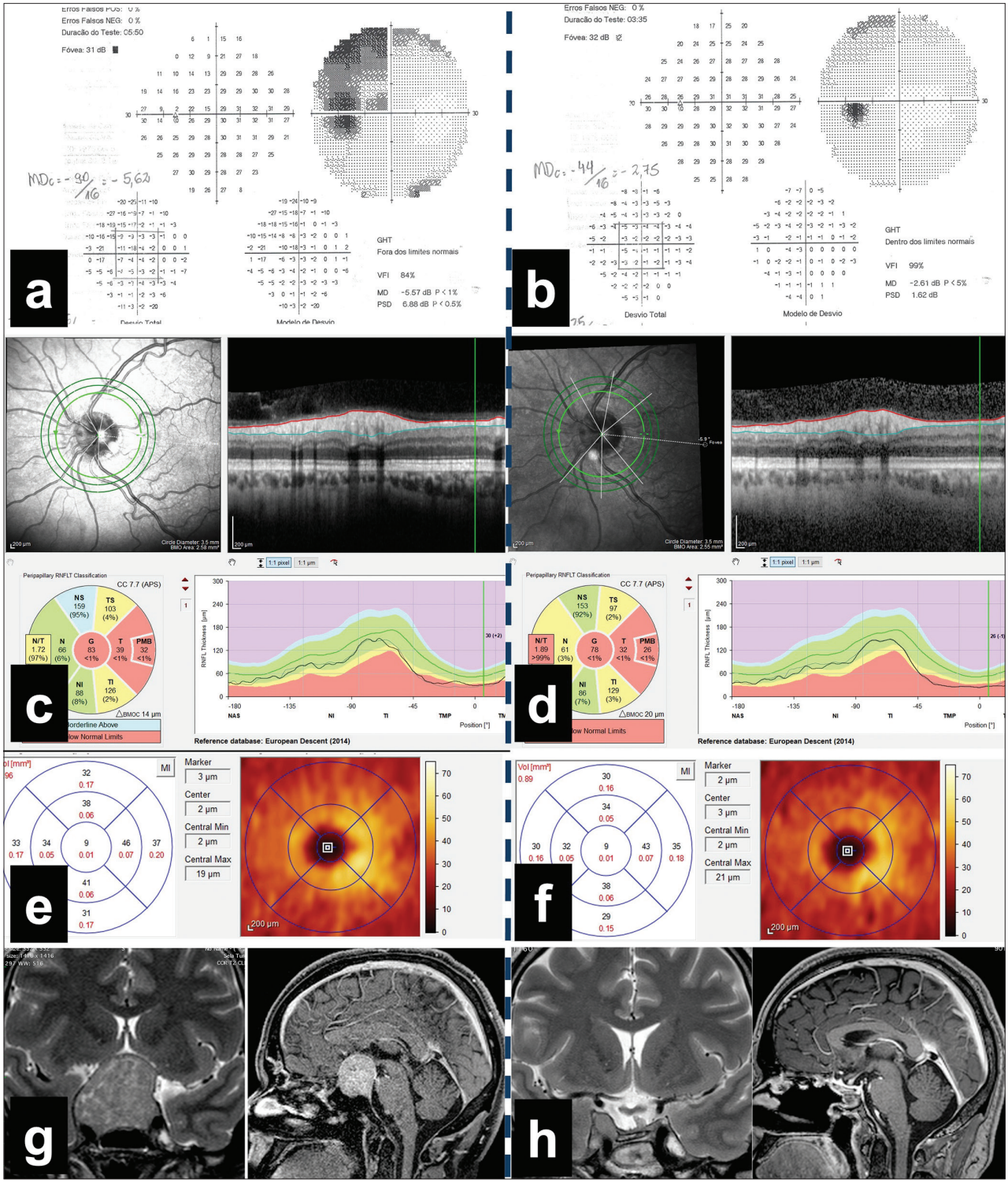
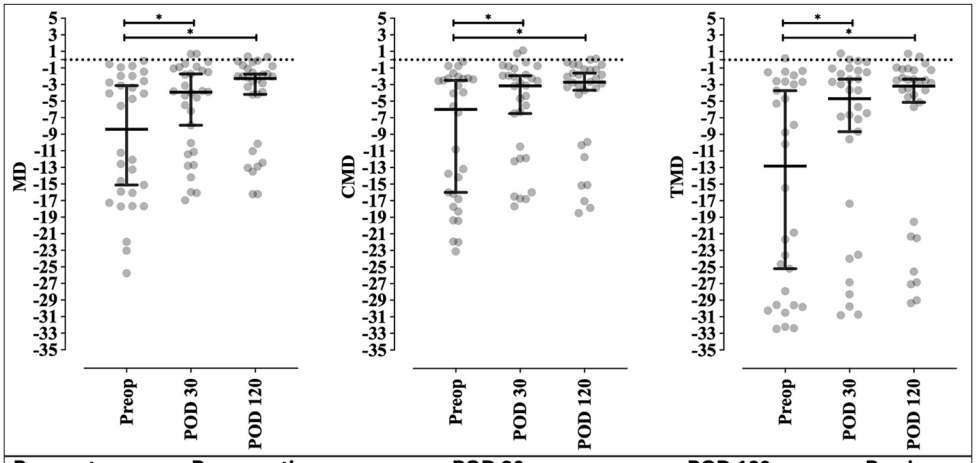


Figure 4: Case illustration. Preoperative (left) and postoperative studies (right) – separated by the dashed line – of a 45-year-old male patient of the series with nonfunctioning pituitary macroadenoma. (a and b) Computerized visual perimetries showing significant postoperative improvement. (c-f) OCT images, respectively, of peripapillary retinal nerve fiber layer (c and d) and macular ganglion cell layer (e and f) depicting no significant changes in the thicknesses of different sectors pre and postoperatively. (g and h) Magnetic resonance imaging coronal T2 and sagittal T1 with gadolinium demonstrating total decompression of the optic chiasm and nerves after endoscopic endonasal transsphenoidal resection of the tumor, and a small tumor remnant on the right cavernous sinus.



Parameter	Preoperative	POD 30	POD 120	P-value
MD	-8.41 (-15.11 a -3.39)	-3.93 (-7.73 a 1.77)	-2.27 (-4.06 a -1.78)	<0.001*
CMD	-6.00 (-15.18 a -2.53)	-3.15 (-6.49 a -2.00)	-2.72 (-3.68 a -1.62)	<0.001*
TMD	-12.82 (-24.94 a -4.51)	-4.69 (-7.92 a -2.36)	-3.18 (-4.82 a -2.35)	<0.001*

Figure 5: Graphical demonstration of the evolution of computerized visual perimetry parameters MD, CMD, and TMD from preoperative to POD 30 and POD 120 evaluations. Data are presented as 95% confidence interval of the median. The *P*-values shown in bold* were statistically significant. CMD: Central mean defect, MD: Mean deviation, TMD: Temporal mean defect.

20 years. Visual outcomes are at least comparable to those of the microscopic technique, with some studies showing superior results.[9] In a 2017 meta-analysis of endoscopic surgical series, Muskens *et al*.[23] reported 80.8% perimetric improvement, with 40.4% visual field normalization and 2.3% deterioration. In that study, the authors emphasized that the experience of the surgical team is an important factor for postoperative visual outcome. In our series of patients who were operated on exclusively through the endoscopic endonasal transsphenoidal approach by the same two senior surgeons (neurosurgeon and otorhinolaryngologist) with 15 years' experience with this surgical technique, all eyes with preoperative perimetric deficits showed improvement in at least one parameter (MD, CMD, or TMD) by POD 120. This result confirms the effectiveness of EETR for visual improvement in patients with pituitary macroadenomas.

The results we obtained concerning the correlations of VP and OCT measurements at preoperative and POD 30 and 120 suggest that both peripapillary and macular analyses can reliably assess the severity of compressive optic neuropathy in pituitary macroadenoma cases. Measurements of the macular region seem to be especially reliable since this region contains more ganglion cells and fewer axons, as well as fewer other elements, such as glia and blood vessels, compared to the peripapillary RNFL. Macular measurements, especially those of the ganglion cell and inner plexiform layers, are therefore more accurate indicators of true neuronal loss. They suffer less influence from interstitial edema and axonal engorgement, which can occur in the optic disc. Therefore, macular measurements may be more accurate and reliable indicators of ganglion cell loss[19,20] and have greater predictive value regarding postoperative visual recovery, since true neuronal loss would not allow for significant improvement.

Our findings regarding the postoperative evolution of the thicknesses of both the peripapillary RNFL and macular layers (IPL, GCL, and NFL) studied by OCT revealed significant variation in only two sectors of the 35 sectors studied, the inner superior (SI) and inner nasal (NI) sectors of the NFL of the macula, which showed slight decrease at the postoperative scans. The macular NFL is characterized by its naturally low thickness and there is greater technical variability in its measurements by OCT, which limits the isolated interpretation of these findings. Although late retrograde degeneration has been described in peripapillary RNFL,[6] there are no specific reports involving macular NFL. This finding should therefore be interpreted with caution and requires confirmation in future studies. Conversely, the stability of almost all the OCT parameters in the postoperative outcome is consistent with the postulated inability of ganglion cells and corresponding retinal nerve fibers to regenerate. Certainly, there may be variations in the thickness of the RNFL in some circumstances, including an increase in thickness, as other elements apart from the number of nerve fibers may contribute to thickness measurements, such as in the presence of optic disc edema resulting from intracranial hypertension.[15] In such cases, once the papilledema phase has been resolved, OCT can accurately detect thinning of the RNFL and macular layers resulting from the degenerative process affecting the ganglion cells.[17] However, in the context of a predominantly

Table 2: Evolution of the thicknesses of the different sectors of OCTs along preoperative, POD 30, and POD 120 evaluations.

Sector	Preoperative	PO 30	PO 120	*P*-value
RNFL – PMB	39.60 (34.80 a 44.53)	39.51 (36.14 a 43.09)	40.30 (36.00 a 44.63)	0.417
RNFL – G	86.83 (81.50 a 92.23)	87.22 (82.35 a 91.95)	84.43 (78.23 a 90.36)	0.189
RNFL – NS	109.00 (99.00 a 117.50)	108.37 (103.00 a 119.00)	107.00 (95.51 a 117.50)	0.450
RNFL – TS	116.90 (108.13 a 126.63)	110.29 (102.92 a 117.32)	112.70 (104.30 a 122.46)	0.246
RNFL – T	53.43 (47.80 a 59.33)	52.43 (47.98 a 56.84)	52.70 (47.54 a 58.40)	0.561
RNFL – Ti	144.00 (126.50 a 157.50)	150.50 (140.00 a 154.98)	146.00 (130.50 a 154.50)	0.106
RNFL – Ni	102.23 (91.24 a 114.16)	102.07 (90.67 a 114.19)	100.00 (89.07 a 112.46)	0.295
RNFL – N	67.47 (60.40 a 74.30)	69.05 (62.26 a 75.75)	64.43 (56.80 a 71.56)	0.057
IPL – C	18.00 (17.00 a 20.00)	18.00 (17.00 a 19.84)	18.00 (17.00 a 20.00)	0.783
IPL – SI	36.03 (33.90 a 38.33)	35.35 (33.08 a 37.42)	35.33 (33.00 a 37.83)	0.440
IPL – So	27.00 (25.00 a 28.00)	26.00 (24.26 a 27.00)	26.00 (25.00 a 28.00)	0.961
IPL – NI	33.67 (31.40 a 36.23)	33.66 (31.36 a 35.91)	33.67 (31.30 a 36.33)	0.897
IPL – No	25.83 (24.30 a 27.37)	25.75 (24.22 a 27.26)	25.67 (24.00 a 27.30)	0.859
IPL – II	36.47 (34.30 a 38.70)	35.54 (33.45 a 37.66)	36.07 (33.83 a 38.33)	0.271
IPL – Io	25.07 (23.83 a 26.27)	25.20 (24.08 a 26.30)	25.47 (24.10 a 26.87)	0.151
IPL – TI	39.00 (38.00 a 40.50)	39.21 (37.91 a 41.00)	38.50 (37.00 a 40.00)	0.719
IPL – To	32.50 (31.50 a 34.00)	32.64 (31.84 a 33.79)	32.50 (31.50 a 34.00)	0.380
GCL – C	11.00 (10.00 a 13.00)	11.00 (10.00 a 13.71)	12.00 (10.00 a 13.00)	0.521
GCL – SI	41.40 (37.70 a 45.33)	40.71 (37.02 a 44.40)	41.23 (37.33 a 45.30)	0.280
GCL – So	32.00 (30.00 a 33.00)	31.06 (29.50 a 33.50)	31.50 (30.00 a 34.00)	0.703
GCL – NI	37.37 (33.07 a 41.83)	36.98 (32.99 a 41.25)	37.43 (32.97 a 42.07)	0.728
GCL – No	32.6 (30.53 a 34.80)	32.2 (30.05 a 34.36)	32.23 (29.97 a 34.47)	0.328
GCL – II	42.97 (40.03 a 46.00)	42.02 (39.06 a 44.97)	42.60 (39.14 a 45.90)	0.506
GCL – Io	31.20 (29.77 a 32.57)	31.62 (30.18 a 33.02)	31.27 (29.83 a 32.60)	0.151
GCL – TI	45.50 (42.00 a 46.50)	43.00 (40.89 a 45.00)	43.5 0 (41.00 a 47.50)	0.256
GCL – To	35.00 (33.00 a 37.00)	34.50 (31.64 a 36.00)	35.00 (33.00 a 37.00)	0.444
NFL – C	11.00 (10.00 a 11.50)	11.00 (10.00 a 11.19)	11.00 (10.00 a 11.50)	0.083
NFL – SI	22.9 (21.47 a 24.3)	21.5 (20.47 a 22.47)	21.9 (20.53 a 23.13)	**0.002**
NFL – SO	34.37 (32.43 a 36.57)	32.82 (30.94 a 34.53)	33.10 (30.87 a 35.13)	0.064
NFL – NI	19.00 (18.00 a 20.50)	18.39 (18.00 a 19.03)	18.50 (18.00 a 19.50)	**0.001**
NFL – No	39.77 (360.00 a 43.47)	38.28 (34.89 a 41.62)	37.93 (34.43 a 41.57)	0.062
NFL – II	24.00 (22.50 a 25.00)	22.61 (21.40 a 23.50)	23.50 (22.00 a 24.00)	0.076
NFL – Io	38.27 (35.73 a 40.60)	36.72 (34.54 a 39.01)	37.30 (34.77 a 39.93)	0.139
NFL – TI	17.00 (17.00 a 18.00)	17.11 (17.00 a 18.00)	17.50 (17.00 a 18.00)	0.723
NFL – To	19.00 (19.00 a 19.00)	19.00 (18.00 a 19.70)	19.00 (19.00 a 20.00)	0.074

Data is presented as 95% confidence interval of the median. The *P*-values shown in bold were statistically significant. C: Central or subfoveal area, G: Global, GCL: Ganglion cell layer, II: Inner inferior, IO: Outer inferior, IPL: Inner plexiform layer, N: Nasal, Ni: Inferior nasal NI: Inner nasal, NO: Outer nasal, NS: Superior nasal, OCT: Optic coherence tomography, PMB: Papillomacular bundle, RNFL: Retinal nerve fiber layer, SO: Outer superior, SI: Inner superior, T: Temporal, Ti: Inferior temporal, TI: Inner temporal, TO: Outer temporal, TS: Superior temporal

degenerative process of the nerve fibers, as is the case here (retrograde degeneration caused by chiasmatic or optic nerve compression by the suprasellar tumor), minimal variation in thickness is expected, even after surgical decompression, given nerve fiber or ganglion cells damage that underlies the observed atrophy of RNFL and macular layers is generally considered permanent.[19]

The combination of the findings described above – improvement in the visual field without a corresponding increase in the thickness of the RNFL and macular GCC – confirms reports in the literature suggesting that visual function can recover, particularly in the visual fields, regardless of the persistent thinning of the retinal nerve layers.[29] Indeed, while some studies using OCT have

demonstrated an increase in RNFL thickness in certain sectors following surgical decompression of the optic chiasm,[25] most research indicates a tendency toward stability or minimal variation in these parameters and emphasizes the generally irreversible nature of nerve fiber degeneration and subsequent atrophy of the RNFL and macular layers comprising the GCC.[7,8,14,19] Furthermore, Chung *et al*.[6] demonstrated in a recent study of 268 patients with pituitary adenomas that the peripapillary RNFL may continue to thin over a period of 12–36 months following adequate surgical decompression of the optic apparatus, even in patients exhibiting significant visual improvement as measured by VP. This suggests that, although the process of proximal degeneration of the nerve fibers damaged by the compression of the optic chiasm may continue for months, visual recovery can still occur, probably based on the functional recovery of the nerve fibers that remained intact.

In the present study, all patients with altered OCT scans in the preoperative evaluation also exhibited perimetric deficits, suggesting that OCT is unable to provide an earlier diagnosis of compressive optic neuropathy associated with pituitary macroadenomas. However, this analysis was limited to the peripapillary RNFL. This may explain the discrepancy between our findings and those reported in some studies, which show early alterations detected on OCT in patients with chiasmal compression without visual impairment, since the alterations reported in those studies predominantly referred to macular parameters.[13,29] Tieger *et al*.[29] demonstrated significant thinning of both the GCC (obtained by macular OCT) and the peripapillary RNFL in six patients with normal visual fields in a series of 23 patients with different skull base tumors, with a stronger correlation for the macular parameters. Other publications have also shown that thinning of the GCL and IPL layers may be present in patients with chiasmal compression due to pituitary macroadenomas and normal visual fields, suggesting that loss of retinal ganglion cells may precede perimetric alterations in these patients.[8,18] Blanch *et al*.,[2] in a study of seven patients with sellar tumors and chiasmal compression without campimetric changes, reported that GCC analysis outperformed RNFL analysis. The latter showed only subtle changes in three patients, whereas GCC analysis detected thinning of this layer in all seven patients evaluated. Yum *et al*.,[30] in a study including 31 patients with glaucoma and 46 patients with pituitary macroadenomas, found no RNFL changes in patients with normal VPs, like in the present study. However, these authors reported that alterations in the GCL and IPL were already present in these same patients on macular analysis and emphasized the importance of studying macular parameters for the early diagnosis of compressive optic neuropathy. In a recent study, Bozzi *et al*.[3] detected RNFL alterations in eight out of 20 patients with macroadenomas compressing the chiasm and without visual fields deficits. The authors reported that none of the eight patients exhibited any perimetric deficits during the average 60-month follow-up period. They therefore questioned the validity of RNFL thinning on OCT as an early marker of compressive optic neuropathy.

The reports described above, including the findings of this study, demonstrate that OCT's role in the early diagnosis of optic neuropathy associated with suprasellar pituitary macroadenomas is controversial. In this regard, while assessing the peripapillary RNFL seems to play a limited role, studying macular parameters appears to be the most promising approach and will require further research to determine its value. This, in fact, constitutes the primary limitation of the study, namely the absence of a control group, which would have allowed the determination of normal values for macular GCC sectors and, consequently, the exploration of the role of GCC evaluation in the early diagnosis of compressive optic neuropathy. In this regard, we also acknowledge the small number of patients included for this specific analysis.

A further limitation to be considered is the relatively short follow-up period. The 120-day postoperative period was selected as the time frame for this study, as it allows for the detection of the primary postoperative visual changes that typically occur in patients with pituitary tumors.[11] While the extension of evaluation periods could potentially yield significant additional information, this would require a substantial extension of the study duration. It is our hope that the ophthalmological outcomes of these patients will be re-evaluated in the future and that additional data will be provided. These limitations may be counterbalanced by certain strengths, chiefly represented by the uniformity of patients and both diagnostic and surgical interventions performed in a prospective single-center study.

CONCLUSION

The present study allowed us to confirm that EETR of pituitary macroadenomas provide significant visual improvement to most patients with decreased visual fields. The stability of peripapillary RNFL and most macular layers obtained by OCT, even following visual fields improvement, suggests that postoperative visual functional recovery is independent of the increase in retinal neuronal layers. Our findings also confirm that OCT is capable of adequately detecting signs of compressive optic neuropathy, but peripapillary RNFL analysis did not demonstrate superiority over VP for the early diagnosis in this cohort. Further studies employing OCT for the segmented evaluation of macular GCC, incorporating a control group to provide normative data, with larger sample sizes, might better define its potential role in the early diagnosis and prognosis of the condition, and assist ophthalmologists, endocrinologists, and neurosurgeons in

the preoperative assessment and counseling of patients with pituitary macroadenomas.

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